

### **REMARKS**

Claims 1-16 were pending in the present application. New claims 19-21 have been added to this application by amendment herein. Claims 1-16 and 19-21 are therefore currently pending.

Support for the compounds recited in Claims 19-21 can be found in Table 1 and on page 5, lines 15-26 of the present patent application. In view of this, no new matter has been added to this application by the foregoing amendments.

#### **Response to Restriction Requirement (Election with Traverse)**

The Office Action dated November 6, 2008 required that the Applicant elect a single invention for further prosecution on the merits, selected from the following two groups:

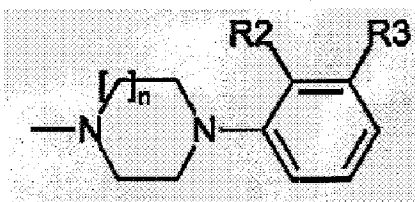
Group I, claims 1-9, drawn to a pharmaceutical composition; and

Group II, claims 10-13, drawn to a method of treatment.

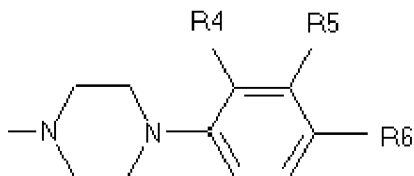
Without conceding the propriety of the restriction requirement, the Applicants provisionally elect Group I, corresponding to claims 1-9. Such election is with traverse and without prejudice to pursue the non-elected claims at a future date in this or in another application. In addition, the Applicants request rejoinder of the non-elected claims should the elected invention be found allowable.

#### **Request for Reconsideration**

The Applicants hereby request reconsideration and withdrawal of the restriction requirement pursuant to 37 CFR § 1.143 on the ground that the compounds recited in claim 1 are both novel and inventive, and therefore that the restricted inventions share a technical relationship. In the Office Action dated November 6, 2008, the Examiner found no special technical relationship or feature common to the restricted inventions because it was asserted that the compounds recited in claim 1 are shown in the prior art, namely in PCT Publication No. WO 03/011396 to Fick. This reference discloses tetrahydroindolone compounds linked to arylpiperazines having the following formula:



By contrast, the arylpiperazine moiety of the compounds recited in claim 1 of the present application (i.e., the R3 group) comprises the following formula:



where R<sub>6</sub> is alkyl, halo, alkoxy, perfluoroalkyl, perfluoroalkoxy, or nitro.

As compared to the compounds disclosed in the Fick reference, in the presently claimed compounds the R<sub>6</sub> position of the arylpiperazine moiety is substituted and is not hydrogen. By contrast, the equivalent position of the compounds disclosed in the Fick reference consists of a hydrogen molecule. The presently claimed compounds are therefore novel in view of the disclosure of the Fick reference.

Moreover, the present compounds have unexpected advantages compared to the compounds of the Fick reference and compared to other compounds of the prior art. In view of this, the present invention therefore makes a contribution over the prior art which comprises an inventive step. This is shown by the results of several tests of the presently claimed compounds which are disclosed in the Declaration of David Helton under 37 CFR § 1.132 (filed with Applicants' Information Disclosure Statement of October 13, 2008). In a model predictive of efficacy in treating the symptoms of schizophrenia, one of the present compounds (1-{4-[4-(3,4-dichlorophenyl)piperazin-1-yl]butyl}-1,5,6,7-tetrahydroindol-4-one) was found to reverse symptoms of schizophrenia with a potency similar to that of clozapine, a drug currently used for treating schizophrenia, but with fewer side effects. In addition, five other compounds of the present invention were also found to have such efficacy (see Table 2 of the Declaration of David Helton).

In a test of the oral availability of pharmaceutical compositions, one of the present compounds (1-{4-[4-(3,4-dichlorophenyl)piperazin-1-yl]butyl}-1,5,6,7-tetrahydroindol-4-one) was also found to have significantly better oral availability compared to compounds of the Fick

reference. Table 1 and Figure 4 of the Declaration of David Helton show that this compound achieved a maximum concentration in blood plasma of 212.3 ng/ml following oral administration, while two compounds of the Fick reference achieved maximum concentrations of only 113.7 and 116.3 ng/ml, respectively. The Fick compounds thus had an oral availability of only a little more than half that of the tested compound of the present invention.

In view of the special relationship between the restricted inventions, the Applicants respectfully request that the restriction requirement in the present application be withdrawn.

### **Election of Species**

The Office Action dated November 6, 2008 further required that one species of the elected invention be selected for prosecution on the merits. In particular, the Applicants were required to elect a particular compound of formula I. The Applicants hereby elect the compound 1-{4-[4-(3,4-dichlorophenyl)piperazin-1-yl]butyl}-1,5,6,7-tetrahydroindol-4-one.

### **Conclusion**

The Examiner is encouraged to contact the undersigned at the telephone number listed below to discuss any questions regarding the present response. If any additional fees are due in connection with the present communication, please charge such fees, or credit any overpayment, to Deposit Account No. 19-2090.

Respectfully submitted,

SHELDON MAK ROSE & ANDERSON

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By: /michael fedrick/  
Michael Fedrick  
Reg. No. 36,799

100 Corson Street, Third Floor  
Pasadena, California 91103-3842  
(626) 796-4000  
Customer No. 23676